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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/563,601	05/04/2006	Bernard Piere Dominique Carcy	I-2003.005 US	8856

31846 7590 04/16/2009

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PATENT DEPARTMENT
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EXAMINER	
ARCHIE, NINA	

ART UNIT	PAPER NUMBER
1645	

NOTIFICATION DATE	DELIVERY MODE
04/16/2009	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/563,601	CARCY ET AL.	
	Examiner	Art Unit	
	Nina A. Archie	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *1/15/2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-21* is/are pending in the application.

4a) Of the above claim(s) *3,6 and 16-18* is/are withdrawn from consideration.

5)☒ Claim(s) *1,2,4,5,7-10 and 19-21* is/are allowed.

6)☒ Claim(s) *11-15* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. This Office is responsive to Applicant's amendment and response filed 1-15-09. Claims 1, 4, 7, and 11 have been amended. Claims 1-21 are pending. Claims 3, 6, and 16-18 have been withdrawn..Claims 1-2, 4-5, 7-15, and 19-21 are currently under examination.

Rejections Withdrawn

2. In view of the Applicant's amendment and remark following objections are withdrawn.

a) Rejections to claims 4-5, 7, and 10 under 35 USC 101, are withdrawn in light of applicant's amendment.

b) Rejections to claim 9 under 35 U.S.C. 102(b) for being anticipated by Vettore et al. is withdrawn in light in light of applicant's amendment and in light of applicants argument.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. The rejection of claims 11-15 under 35 U.5.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contain subject matter, which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention is maintained for the reasons set forth in the previous office action.

Applicant arguments:

Applicants arguments filed in response to the claims 11-15 under 35 U.5.C. 112, first paragraph, on January 15, 2009 is carefully considered, but not found to be persuasive for the reasons below.

A) The amendment to claim 1 overcomes the rejection.

Examiner's Response to Applicant's Argument

In response to applicant's statement in (A), the specification is not enabled for any vaccine comprising an isolated amino acid sequence comprising amino acids 17 to 233 of SEQ ID NO: 2, wherein said sequence provides prophylactic or therapeutic treatment of any type of infection as discussed in the previous office action. The specification is limited to the reduction of *Babesia canis* parasites in erythrocyte cultures with alpha-His-Bc28.1C (see pgs. 48-54). Although claim 11 has been amended, the claims encompass all vaccines comprising an isolated amino acid sequence comprising amino acids 17 to 233 of SEQ ID NO: 2. However, the specification gives no guidance as to what pathogen a given vaccine has efficacy. For example the vaccine as presently claim can be comprising any type of species such as species in the *Babesiidae* family and also other species comprising *Toxoplasma gondii, Besnoitia bennetti, Besnoitia besnoiti, Besnoitia tarandi, Sarcocystis, Neospora, and all Bab*. The claimed invention is not limited to a particular vaccine.

Also, there is no data regarding the induction of a protective immune response to a given pathogen disclosed. The data as set forth in the specification (pgs. 47-54) does not demonstrate that the composition confers "protection" against infection by any species in the *Babesiidae* family but also other species comprising *Toxoplasma gondii, Besnoitia bennetti, Besnoitia besnoiti, Besnoitia tarandi, Sarcocystis, Neospora, and all Bab*. Therefore the data fails to show treatment or vaccine protection against any other species. Therefore, one skilled in the art would not accept on its face the examples given in the specification as being correlative or representative of a successful model. The working examples do not disclose any empirical data or results indicative of a vaccine comprising an isolated amino acid sequence in amino acids 17 to 233 of SEQ ID NO: 2 as claimed. Furthermore, the specification does not disclose any working example that any vaccine further comprising any additionally immunoactive component or a nucleic acid encoding an immunuoactive component as claimed will work against any type of infection or vaccine protection with amino acids 17 to 233 of SEQ ID NO: 2.

Furthermore an isolated amino acid sequence in amino acids 17 to 233 of SEQ ID NO: 2, is a sequence comprising a fragment which have different possibilities of changes to the amino acid. Therefore it is hard for one skilled in the art to determine if the vaccine as claimed can be protective against any subject. A vaccine by definition must provide protection against an infection demonstrable by challenge experiments. The specification is devoid of any teaching that the claimed vaccine comprising an isolated amino acid sequence in amino acids 17 to 233 of SEQ ID NO: 2 nor does the specification disclose a protective response against any subject. Therefore the rejection is maintained.

As outlined previously, the specification is not enabled for vaccine comprising an isolated amino acid sequence from 17 to 233 of SEQ ID NO: 2, wherein said sequence provides prophylactic or therapeutic treatment of any type of infection.

Enablement is considered in view of the Wands factors (MPEP 2164.01(a)). There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue." These factors include, but are not limited to:

(A) The breadth of the claims;

(B) The nature of the invention;

(C) The state of the prior art;

(D) The level of one of ordinary skill;

(E) The level of predictability in the art;

(F) The amount of direction provided by the inventor;

(G) The existence of working examples; and

(H) The quantity of experimentation needed to make or use the invention based on the content of the disclosure.

The breadth of the claims

The claim is drawn to vaccine comprising an isolated amino acid sequence from 17 to 233 of SEQ ID NO: 2 being used for prophylactic or therapeutic treatment of any type of infection is overly broad. Therefore it is hard for one skilled in the art to determine if a vaccine isolated amino acid sequence from 17 to 233 of SEQ ID NO: 2, wherein said sequence provides prophylactic or therapeutic treatment of any type of infection. The quantity of experimentation required to practice the invention as claimed would require in vivo and in vitro studies of an isolated amino acid sequence from 17 to 233 of SEQ ID NO: 2, wherein said sequence provides prophylactic or therapeutic treatment of any type of infection. Since the specification fails to provide particular guidance for a isolated amino acid sequence from 17 to 233 of SEQ ID NO: 2, wherein said sequence provides prophylactic or therapeutic treatment of any type of infection, it would require undue experimentation to practice the invention over the broad scope as presently claimed.

Nature of the invention

The claims are drawn to a vaccine comprising isolated amino acid sequence from 17 to 233 of SEQ ID NO: 2, wherein said sequence provides prophylactic or therapeutic treatment of any type of infection. The specification discloses in Example 3 (see pp. 48), vaccinations with Bc28.1 and Bc28.2 protein subunit vaccine.

Guidance in the specification/Working Examples

The specification fails to provide an enabling disclosure for a vaccine isolated amino acid sequence from 17 to 233 of SEQ ID NO: 2, wherein said sequence provides prophylactic or therapeutic treatment of any type of infection. The specification provides no disclosure how any isolated amino acid, may be used as a vaccine because it fails to provide guidance whether this variant has the ability to induce a protective immune response or to bind to antisera from infected animal. Absent such demonstration, the invention would require undue experimentation to practice as claimed. The specification, however, provides no working examples demonstrating (i.e., guidance) enablement for

vaccine, an isolated amino acid sequence from 17 to 233 of SEQ ID NO: 2, wherein said sequence provides prophylactic or therapeutic treatment of any type of infection.

The state of the prior art

The state of the art indicate as set forth by Plotkin et al (VACCINES W.B. Saunders Company, 1988, page 571) "The key to the problem (of vaccine development) is the identification of that protein component of a virus or microbial pathogen that itself can elicit the production of protective antibodies… and thus protect the host against attack by the pathogen." This teaching of the instant claims directly addresses whether any isolated amino acid sequence, wherein said sequence provides prophylactic or therapeutic treatment of any type of infection. Furthermore, A vaccine "must by definition trigger an immunoprotective response in the host vaccinated; mere antigenic response is not enough." In re Wright, 999 F.2d 1557,1561, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993). The state of the art indicate that any substitution, insertion or deletion or change in an amino acid sequence or nucleic acid that encodes an amino acid highly complex and unpredictable. As taught by the prior art that even a single amino acid change in a protein leads to unpredictable changes in the biological activity of the protein. For example, replacement of a single lysine residue at position 118 of the acidic fibroblast growth factor by glutamic acid led to a substantial loss of heparin binding, receptor binding, and biological-activity of the protein (Burgess et al., The Journal of Cell Biology, 111:2129-2138, 1990). Thus, it is apparent that change in a peptide leads to loss of binding property of that peptide. Furthermore, it is unclear whether the amino acid can be used for prophylactic or therapeutic treatment of any type of infection. It is known for nucleic acids as well as proteins, for example, that even a single nucleotide or amino acid change or mutation can destroy the function of the biomolecule in many instances, albeit not in all cases. The effect of these changes are largely unpredictable as to which one have significant effect versus not. Therefore, the citation of sequence similarity results in an unpredictable and therefore unreliable correspondence between the claimed biomolecule and the indicated similar biomolecule of known function and therefore lacks support regarding utility and/or enablement. Bowie et al teach that an amino acid

sequence encodes a message that determines the shape and function of a protein and that it is the ability of these proteins to fold into unique three-dimensional structures that allows them to function, carry out the instructions of the genome and form immunoepitopes. Bowie et al. further teach that the problem of predicting protein structure from sequence data and in turn utilizing predicted structural determinations to ascertain functional aspects of the protein is extremely complex. (column 1, page 1306). Bowie et al further teach that while it is known that many amino acid substitutions are possible in any given protein, the position within the protein's sequence where such amino acid substitutions can be made with a reasonable expectation of maintaining function are limited. Certain positions in the sequence are critical to the three dimensional structure/function relationship and these regions can tolerate only conservative substitutions or no substitutions (column 2, page 1306). Several publications document this unpredictability of the relationship between sequence and function, albeit that certain specific sequence may be found to be conserved over biomolecules of related function upon a significant amount of further research. See the following publications that support this unpredictability as noting certain conserved sequences in limited specific cases: (Gerhold et al [BioEssays, Vol.18, pages. 973-981 {1996}] Bowie et al (Science, 1990, 247:1306-1310). For the reasons set forth supra, the state of the art is unpredictable of any isolated amino acid sequence, wherein said sequence provides prophylactic or therapeutic treatment of any type of infection.

In conclusion, the claimed inventions are not enabled for a vaccine isolated amino acid sequence from 17 to 233 of SEQ ID NO: 2, wherein said sequence provides prophylactic or therapeutic treatment of any type of infection. The specification discloses in Example 3 (see pp. 48), vaccinations with Bc28.1 and Bc28.2 protein subunit vaccine. The state of the art indicate that any substitution, insertion or deletion or change in an amino acid sequence or nucleic acid that encodes an amino acid highly complex and unpredictable. There is a lack of working examples. As a result, for the reasons discussed above, it would require undue experimentation for one skilled in the art to use the claimed invention.

Conclusions

4. No claims are allowed.

5. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nina A. Archie whose telephone number is 571-272-9938. The examiner can normally be reached on Monday-Friday 8:30-5:00p.m..

If attempts to reach the examiner by telephone are unsuccessful, the examiner supervisor, Robert Mondesi can be reached on 571-272-0956. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO

Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Nina A Archie
Examiner
GAU 1645
REM 3B31

/Robert A. Zeman/
for Nina Archie, Examiner of Art Unit 1645